Informed Consent for Biobanking

Laura M. Beskow, MPH, PhD

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Importance of Biobanking

- **The vision of "personalized medicine" is to improve the standard of medical care by including an individual's genetic and molecular information in the clinical decision-making process… Human biospecimens are the fuel that drives the basic and translational research needed to achieve this vision**

  Vaught et al (2011)

- **Biobanks are the infrastructural equivalent of linear accelerators and telescope arrays … that is, broad-based platforms to support the scientific community in its asking and answering of key questions across the realm of bioscience**

  Murtagh et al (2011)

Public Support for Biobanking

- **Data suggest that people are supportive of biobanking research**
  - **A large survey (n=4659) about a US biobank found that "widespread support exists in the general public for a large national cohort study" (Kaufman et al, 2008)**
    - **84% supported the study, 60% would participate**
- **Found in studies of specimens collected for clinical purpose as well as specimens collected for research**

See Vermeulen et al (2009), Kaufman et al (2009), Beskow & Dean (2008), Bryant et al (2008), Hamilton et al (2007), Wendler (2006)

Biobanking Consent is Challenging

- **“Minimal risk” but…**
  - **Unspecified future research**
  - **Indefinite storage**
  - **Access to medical records**
  - **Contact for future research**
  - **Large-scale sharing**
  - **Development of commercial products**
  - **Confidentiality protections**
  - **Access to research results**
  - **Ability to withdraw**

Informed Consent in General is Challenging!

- **Individuals should understand the purpose, procedures, risks, benefits, and alternatives, and make a voluntary decision**
- **Studies document problems in clinical research as well as biobanking research in particular**

Informed Consent in General is Challenging, continued

- **In two separate studies of biobanking consent, >1/3 of participants answered questions incorrectly regarding:**
  - **The purpose of the research**
  - **Limitations to confidentiality protections**
  - **That their DNA would be stored**
  - **That the research involved some risks**
  - **Whether they would receive individual genetic results**

McCarty et al (2007), Ormond et al (2009)

Consent Form Problems

Deficiencies in 3 major areas:

- **Missing elements**
- **Readability**
- **Length**

The evolution of consent forms for research (2010)

Longer consent forms for clinical trials compromise patient understanding: so why are they lengthening? (2007)

Consent document for oncology trials: does anybody read these things? (2004)

Readability standards for informed consent forms as compared with actual readability (2003)

Informed consent for medical research: common discrepancies and readability (1996)

Are informed consent forms that describe clinical oncology research protocols readable by most patients and their families? (1994)

Research consent forms: continued unreadability and increasing length (1989)

Consent Form Problems, continued

Consent forms are "becoming ever more intimidating, and perhaps inhibiting rather than enhancing participants' understanding. Participants may not even read them, much less understand them."

Hastings Center Report (2008)

Today's Discussion

- **Prospective participants' values and perceptions regarding consent for biobanking research**
  - **Overview of the literature**
- **Differences among investigators, IRB, participants regarding priorities for biobanking consent**
  - **Results of empirical study**
- **Resources for developing appropriate consent strategies for biobanking research**

Part 1

BIOBANKING CONSENT: PARTICIPANT VALUES AND PERCEPTIONS

People Want to Be Asked

- **People typically want to be asked whether their specimens can be used for research**
  - **A survey (n=751) about a proposed biobank at a major academic medical center found that 67% preferred opt-in over opt-out or no consent (Simon et al, 2011)**
    - **Allows for positive and active choice; more informative; greater public acceptance; opinions respected & valued**
- **Found in studies of specimens collected for clinical purpose as well as specimens collected for research**

See Murphy et al (2009), Vermeulen et al (2009), Hamilton et al (2007)

Many Accept Broad Consent for Future Research Use

- **Beyond initial consent, many do not want significant control over how specimens are used**
  - **In Simon et al (2011), broad consent preferred over categorical and study-specific consent models**
    - **Allows for flexibility in research; logical given uncertainty of future research; logistically easier; spur research output**
- **Found in studies of specimens collected for clinical purpose as well as specimens collected for research**

See Simon et al (2011), Lipworth et al (2009), Treweek et al (2009), Vermeulen et al (2009), Hamilton et al (2007), Kaphingst et al (2006), Wendler (2006)

Many Accept Broad Consent for Future Research Use, continued

- However, certain contexts where this is notably NOT the case
- Example: Havasupai case
  - In 2010, ASU agreed to pay $700,000 to settle claims that university researchers improperly used tribe members' blood samples in genetic research
  - "When research involves a defined community, community consultation during study planning can help to identify areas of concern regarding possible future uses of biospecimens" (Mello & Wolf 2010)

People Want To Know That Their Contributions Are Put To Good Use

- **Example: One interviewee about a proposed Duke Biobank (Beskow & Dean 2008):**

  "I would like to know what happened. I mean, did it help? I would like to know what they're focusing on, what they're finding out. Just to see the result, to know that this research is contributing to something, helping somebody or society."

- **Suggests role for better communication with participants *and* general public about studies being done and things being learned**

See Beskow et al (2012)

Context Matters

- **People "will acquire different expectations dependent on the type of biobank they contribute to and the recruitment process they engage in" (Hoeyer 2010)**
- **Biobanks are not homogeneous entities**
  - **Constructed with specimens originally collected for different purposes (clinical vs. research)**
  - **Established and run by different entities (e.g., physicians, patient groups, population-based cohort studies)**
  - **Accessed by different researchers (e.g., industry, academic)**
  - **Operated on different terms and conditions**

Context Matters, continued

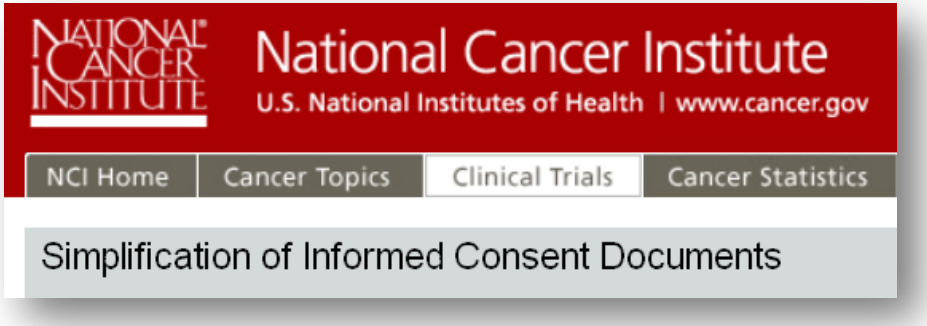
- **Further, biobanks can:**
  - **Collect different tissue types (e.g., tumor tissue vs. blood)**
  - **Procured from people in different situations (e.g., patients vs. healthy participants)**
  - **Exist in different geographical, social, and historical contexts**
- **Thus, it is unlikely that a one-size-fits-all approach can be taken to developing policies for how biospecimens and data are collected and used for research**

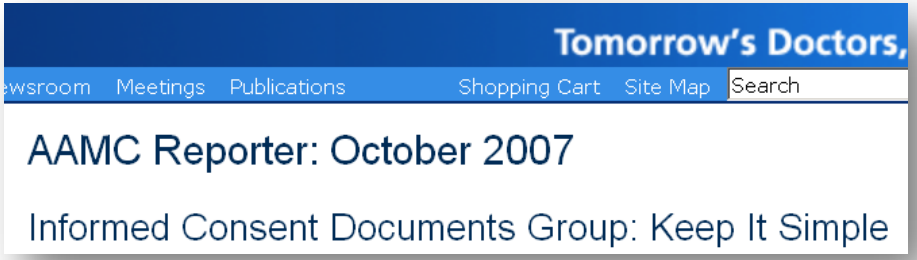
Therefore … ?

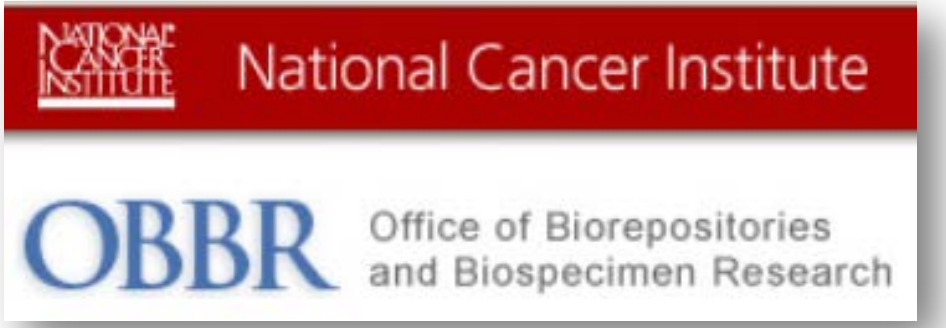
- **Despite no one-size-fits-all approach, safe to assume people want concise, understandable information**
  - **Prospective participants "want to spend as much time as necessary, but no more, obtaining information and making a decision about taking part in research" (Beskow et al, 2010)**
- **Idea of a concise, easy-to-read consent form consistent with:**
  - **Calls to simplify consent forms in general**
  - **Recent 'Advance Notice of Proposed Rulemaking'**

OBBR 2007 Workshop:

- 1-page consent form outlining important issues and risks in straightforward language
- More detailed supplementary materials should be made available to interested participants







ANPRM: Enhancing Protections For Research Subjects

- **Proposal to clarify procedures and enhance protections related to research with biospecimens:**
  - **In almost all cases, persons would have the right to allow or disallow the use of their biospecimens for research, regardless of whether the specimens were initially collected for research purposes or as part of clinical care**
  - **Includes a suggestion that a standard, brief, and general form be used to obtain consent for the future open-ended use of biospecimens in research**

Emanuel & Menikoff (2011)

Simplified Forms: The Challenge

- **Determining material information that a reasonable person would want to know**
  - **As opposed to unnecessary detail that may confuse and detract**
- **What patients and research subjects find essential may differ from information identified as important by “experts”**

Part 2

BIOBANKING CONSENT: DIFFERENCES AMONG INVESTIGATORS, IRB, AND PROSPECTIVE PARTICIPANTS

Empirical Study

- **Beskow LM, Friedman J, Hardy C, Lin L, Weinfurt KP. Simplifying informed consent for biorepositories: stakeholder perspectives. *Genetics in Medicine* 2010; 12(9): 567-72**

Project Team

- Laura Beskow, Principal Investigator
- Kevin Weinfurt, Co-Principal Investigator
- Joëlle Friedman, Study Coordinator
- Chantelle Hardy, Research Assistant
- Li Lin, Statistician
- Ashley Dunham, MURDOCK Community Health Project Leader
- Laveina Dash, MURDOCK Study Clinical Research Coordinator
- Whitney McLeod, Research Assistant

Funded by the MURDOCK Study

Methods

- **Research participants**
  - **Mailing to stratified random sample from physician practice databases in Durham and Kannapolis, NC**
  - **Purposive enrollment to achieve diversity by sex, race, age, education**
  - **Half assigned to read 6+ page form = 52**

Methods, continued

- **Duke & Kannapolis IRB chairs/members**
  - **20 / 25 = 80%**
- **MURDOCK Study investigators**
  - **12 / 12 = 100%**

6+ Page Form Readability Characteristics

- **Flesch-Kincaid grade level: 8.0**
  - **Ideally 8 or below**
- **Flesch reading ease: 63.5**
  - **Higher is better; ideally 60-70**
- **Passive sentences: 16%**

Methods, continued

- **“As you go through the form this time, we would like you to highlight the sentences that — in your opinion — contain the most important information about taking part in a biobank. In other words, highlight the sentences that have information that would matter most to you, if you were thinking about taking part in a biobank.”**

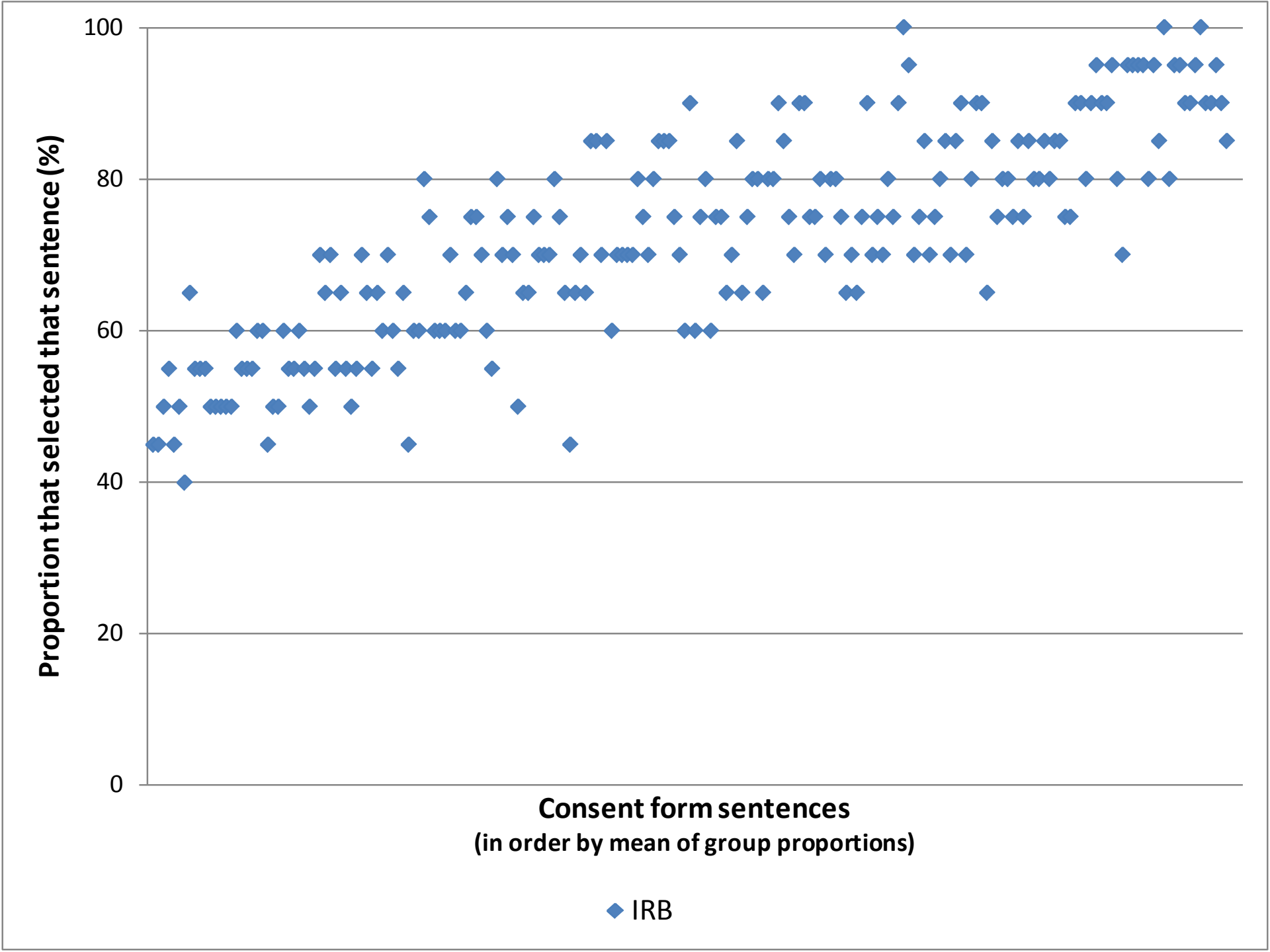
Participant Characteristics

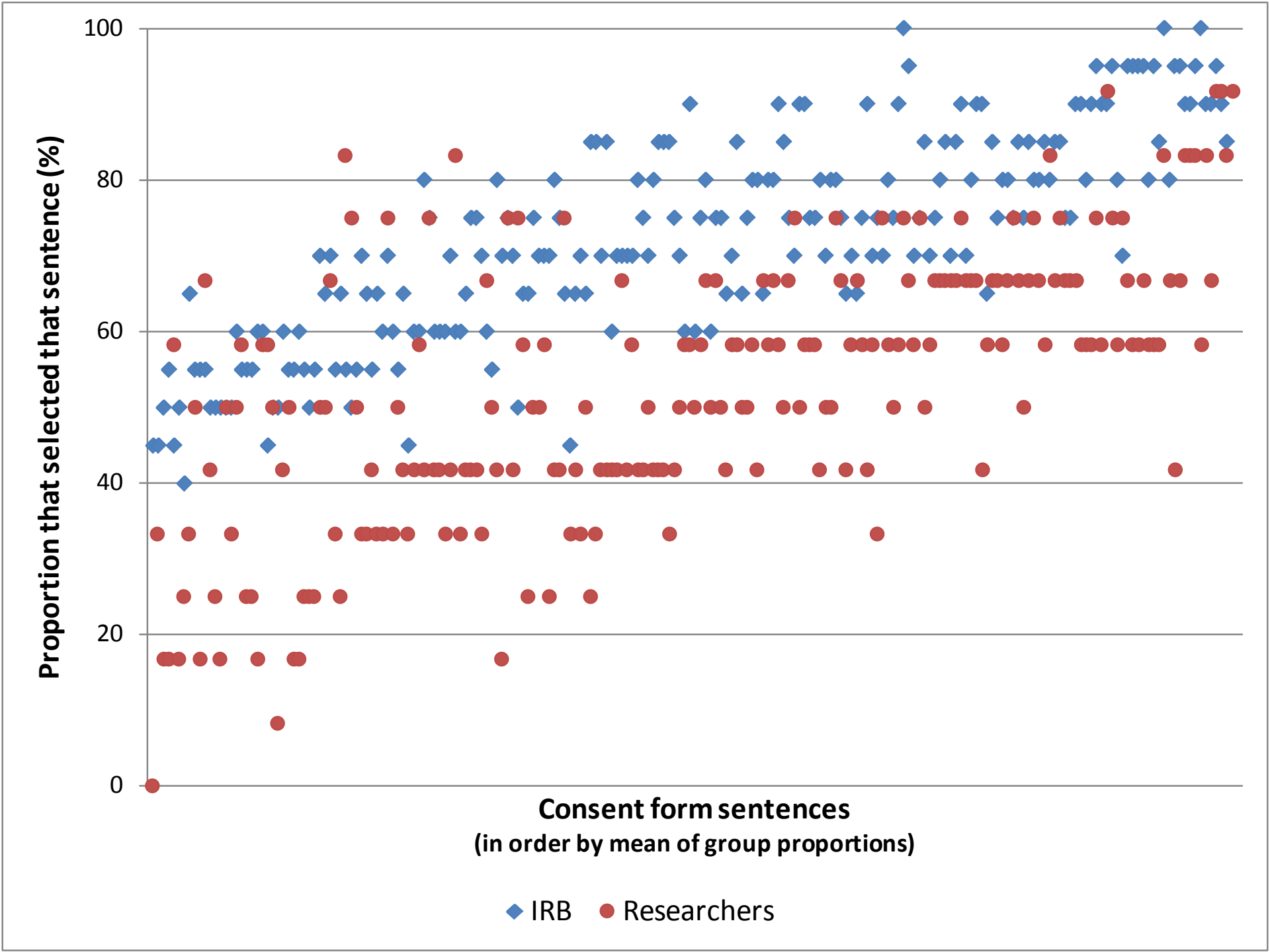
	Participants (N = 52)		Researchers (N = 12)		IRB (N = 20)	
	n	%	*n*	%	*n*	%
Age, years						
<55	13	(25.0)	9	(75.0)	13	(65.0)
55+	39	(75.0)	3	(25.0)	7	(35.0)
Sex						
Female	30	(57.7)	6	(50.0)	9	(45.0)
Male	22	(42.3)	6	(50.0)	11	(55.0)
Ethnicity (Hispanic)						
No	52	(100.0)	11	(91.7)	20	(100.0)
Yes	0	(0.0)	1	(8.3)	0	(0.0)
Race						
White	43	(82.7)	9	(75.0)	20	(100.0)
Other than white	9	(17.3)	3	(25.0)	0	(0.0)
Education Level						
Less than bachelor's degree	26	(50.0)	*		*	
Bachelor's degree or higher	26	(50.0)	*		*	

** Educational attainment was not collected for researchers and IRB representatives.*

Number of Sentences Selected as Important

- **Mean selected out of 207 sentences:**
  - **Research participants 83.7 (40%)**
  - **Researchers 109.8 (53%)**
  - **IRB 149.7 (72%)**
- **IRB highlighted significantly more sentences than did participants ($p<0.0001$)**
  - **IRB vs. researchers ($p=0.07$)**
  - **Researchers vs. participants ($p=0.18$)**


100
80
60
40
20
0
Proportion that selected that sentence (%)
Consent form sentences
(in order by mean of group proportions)
IRB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IRB
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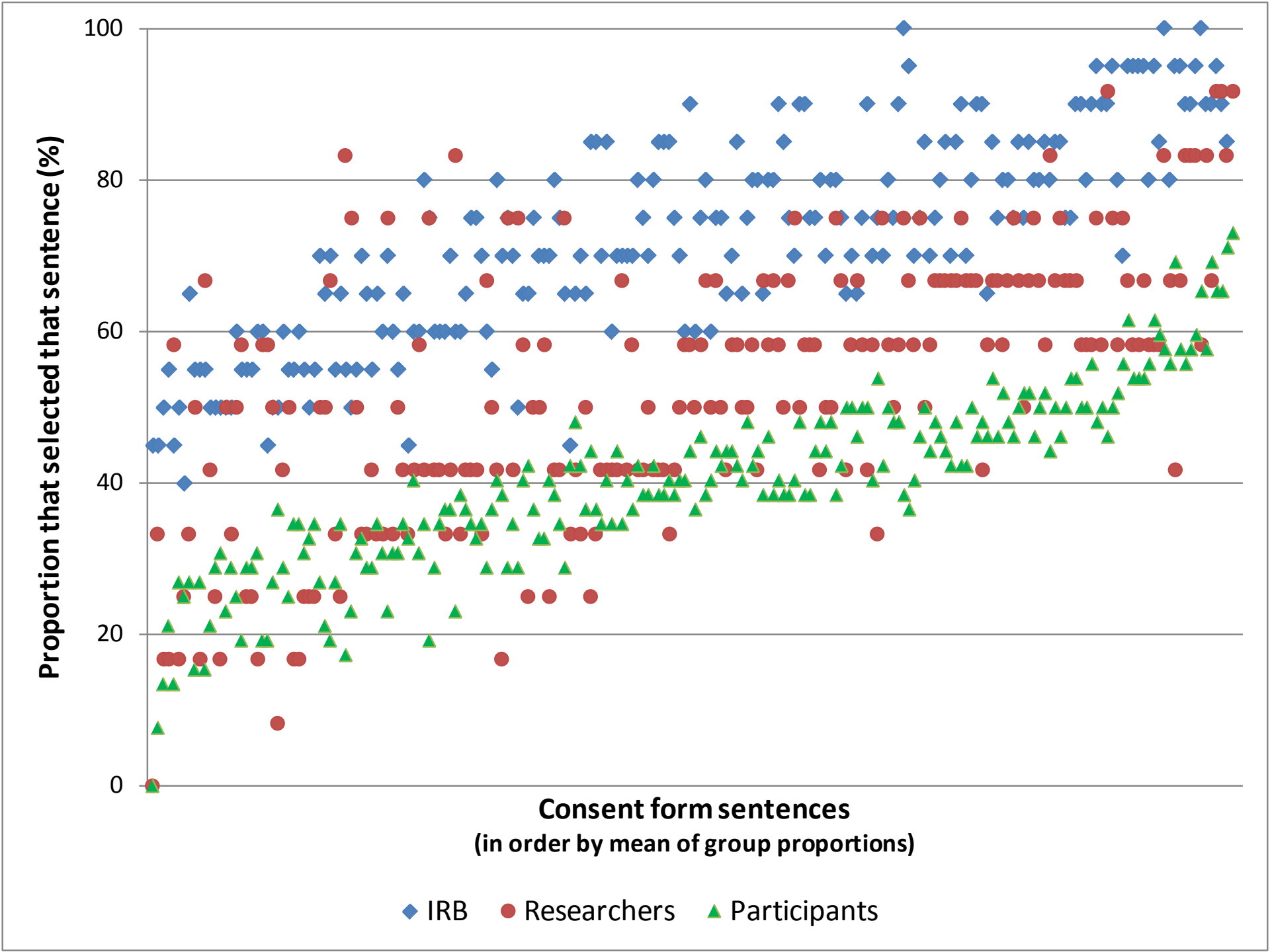
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80
60
40
20
0
Proportion that selected that sentence (%)
Consent form sentences
(in order by mean of group proportions)
IRB
Researchers
Participants

Rankings: Topics of Sentences Most Often Selected

Topic	Participants	Researchers	IRB
Purpose			
Voluntariness			
Right to Refuse			
Biospecimen Collection			
Collection of Basic Information			
Medical Record Access			
Duration of Storage			
Research Recontact			
Large-Scale Data Sharing			
Privacy Risks			
Privacy Protections			
Costs & Payments			
Individual Research Results			
Options			
Right to Withdraw			

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Options			
Right to Withdraw			

"We will not give researchers your name or any other information that could identify you without your permission."

Proportions: Agreement

- **No significant difference in proportions of each group that selected sentences about:**
  - **Large-scale data sharing**
  - **Privacy risks**
  - **Privacy protection of not placing research data in medical records**
  - **Narrow circumstances in which individual research results would be offered to participants**

Proportions: Disagreement

- **Sentences IRB selected significantly more often than participants, researchers:**
  - **Collection of basic demographic information, family health history**
  - **Unlimited length of time specimens/data stored**
  - **Summary of optional aspects of biorepository participation**
  - **Options that would be available to participants who wanted to discontinue participation**

Proportions: Disagreement, con't

- **Sentences IRB, researchers selected significantly more often than participants:**
  - **Purpose of the biorepository**
  - **Collection of basic personal information**
  - **Re-contact about additional research**
  - **Individual research results not offered as a matter of routine**

Potential Sources of Differences

- **Differing mandate for each group**
  - **Participants: Information reasonable person needs to make informed, voluntary decision**
  - **Researchers: Meet IRB requirements, plus first-hand experience with consent process**
  - **IRB: Protect participants, regulatory compliance, institutional liability**
- **Competing motivations may impede efforts to get simplified forms into practice**

Comparing Perspectives: Some Other Examples

- **Genetic research review**
  - **Edwards KL, Lemke AA, Trinidad SB, Lewis SM, Starks H, et al. Genetics researchers' and IRB professionals' attitudes toward genetic research review: a comparative analysis. *Genet Med* 2012;14:236-42.**
    - A majority of both groups agreed that reconsent should be required in 4 of 6 scenarios presented.
    - More genetic researcher respondents trusted confidentiality of coded data, fewer expected harms from reidentification, and fewer considering reconsent necessary in certain scenarios.

Comparing Perspectives: Some Other Examples

- **Genotype-driven research recruitment**
  - **Beskow LM, Namey EE, Miller PR, Nelson DK, Cooper A. IRB chairs' perspectives on genotype-driven research recruitment. *IRB* 2012; in press.**
  - **Beskow LM, Namey EE, Cadigan RJ, Brazg T, Crouch J, et al. Research participants' perspectives on genotype-driven research recruitment. *J Empir Res Hum Res Ethics* 2011;6:3-20.**
    - **Not direct comparison, but asked both groups about the importance of consent disclosures and choices regarding recontact about participation in additional research**

Part 3

RESOURCES TO DEVELOP APPROPRIATE BIOBANKING CONSENT STRATEGIES

Overview

- Resources to help enhance and simplify biobanking consent forms
  - Model forms
  - Other resources
- Resources on participant perspectives
- Some ideas for gathering community input

Model Forms

- **Beskow LM, Friedman J, Hardy C, Lin L, Weinfurt KP. Developing a simplified consent form for biobanking. *PLoS One* 2010; 5(10): e13302.**
  - **http://dx.plos.org/10.1371/journal.pone.0013302**
  - **2-page model form (7th grade reading level)**
  - **Itemized rationale for content**
  - **Preliminary feedback from participants**

Model Forms, continued

- **Electronic Medical Records & Genomics (eMERGE) Network model consent language for biobanking**
  - **http://www.genome.gov/27526660**
  - **Customizable model language**
- **Cooperative Group Banking Committee**
  - **http://cgb.cancer.gov/**
  - **Forthcoming: Model consent form, patient education brochure, IRB info sheet**

Other Consent Form Resources

'Best Practice' content:

- **NCI Best Practices for Biospecimen Resources (2011)**
- **ISBER Best Practices for Repositories (2008)**
- **RAND Best Practices for a Biospecimen Resource for the Genomic and Proteomic Era (2003)**
- **NBAC - Research Involving Human Biological Materials: Ethical Issues and Policy Guidance (1999)**
- **NIH - Genome-Wide Association Studies: Points to Consider for IRBs and Institutions (2011)**
- **McGuire AL, Beskow LM. Informed consent in genomics and genetic research. *Annu Rev Genomics Hum Genet* 2010; 11: 361-81**

Group Health's Program for Readability In Science & Medicine (PRISM)

http://www.grouphealthresearch.org

Resources on Participant Perspectives

- Rapidly growing body of literature documenting participant perspectives
  - e.g., biobanking in general, consent, need for re-consent, data sharing, identifiability, access to individual results
- Be a critical reader
  - What is the role of data on participant views in development of policies, practices?
  - Limitations in empirical research

Resources on Participant Perspectives, continued

- Some common limitations
  - Small sample sizes, generalizeability
  - Non-randomized designs
  - Hypothetical or simulated settings
  - Definition of concepts, background education
  - Measures
- These do not negate findings, but be aware of implications

Ideas for Gathering Community Input

- **Caution in defining biobank 'community'**
  - **Ross et al (2010): Established communities with internal structure, identifiable leadership *versus* groups of individuals with a shared characteristic**
- **Some possibilities:**
  - **Clinician who regularly works with patients with the condition under study**
  - **Disease- or condition-specific advocacy organizations**
  - **Simple focus group of potential participants**
  - **Community advisory board**
  - **Community-based participatory research**


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